Remarks

The foregoing amendments to the claims are believed to place the claims into condition for immediate allowance or into better condition for consideration on appeal. Moreover, the amendments merely clarify Applicants' invention and do not raise new issues for consideration by the Examiner. Entry of the present amendment and reconsideration of this application is respectfully requested.

Claims 45, 49, 50, 53-57, 72-75, and 77 have been canceled without prejudice or disclaimer to the subject matter thereof. Upon entry of the foregoing amendments, claims 33-43, 46, 47, 51, 52, 58-61, 71, and 76 are pending in the application, with claims 33, 42, 46, and 58 being the independent claims. Support for the amendment to claims 33, 42, 43, 46, 47, 58, and 74 can be found, *inter alia*, on page 23, line 15 through page 24, line 2 and on page 21, line 24, through page 22, line 4. Support for the amendment to claim 76 can be found on page 19, lines 14 through 23.

No new subject matter is added by way of these amendments. Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Rejections Under 35 U.S.C. § 112, second paragraph

A. First Rejection (Claims 33-41 and 74)

Claims 33-41 and 74 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. (Office Action, page 4). Applicants respectfully traverse this rejection.

The Examiner is of the opinion that:

> The phrases "a disorder responsive to the induction of apoptosis" and "a mammal in need of such treatment" are indefinite. The claims provide for the use of the compounds of formula III, but the claims do not set forth any steps involved in determining how to identify what disorders or mammals are to be treated. It is unclear what diseases and treatments applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how to practice this use. Identifying which diseases applicants intend this claim to cover will involve extensive and potentially inconclusive clinical research. With out such clinical research to identify the patients and diseases applicants intend to treat, one skilled in the art cannot determine the metes and bounds of the claim. Hence, the claims are indefinite.

Applicants respectfully disagree. Claim 74 has been canceled. The claims as amended provide a list of specific disorders that are responsive to the induction of apoptosis. There is no question as to the disorders or mammals that are to be treated or what diseases and treatments are intended to be encompassed by the claims. Thus, claims 33-41 are not indefinite.

B. Second Rejection (Claims 33-38, 40, 42, 43, 45-47, 51-58, 60, 71, and 74-77)

Claims 33-38, 40, 42, 43, 45-47, 51-58, 60, 71, and 74-77 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. (Office Action, page 9). Applicants respectfully traverse this rejection.

The Examiner is of the opinion that:

> The word "prodrug", which occurs in claims 33, 40, 42, 43, 46, 47, 58, 60, 74 and 77 is indefinite. The issue on second paragraph is whether the structures of the claimed compounds are clearly defined. Applicants' "prodrugs" are molecules whose structure lie outside the subject matter of claim 1, but upon metabolism in the body are converted to active compounds falling within the structural scope of claim 1. The claim describes the function intended but provides no specific structural guidance to what constitutes a "prodrug". Structural formulas, names, or both can accurately describe organic compounds, which are the subject matter of claim 1. Attempting to define means by function is not proper when the means can be clearly expressed in terms that are more precise.

Applicants respectfully disagree. Claims 45, 53-57, 74, 75, and 77 have been canceled. The structures of "prodrugs" for the compounds of the invention are defined in the specification at page 21, line 24, through page 22, line 4. The word "prodrug" is a term of art, well known to one of ordinary skill in the art. However, in the interests of advancing the prosecution of this application, claims 33, 42, 43, 46, 47, 58, and 60 have been amended as suggested by the Examiner to more specifically recite the prodrugs intended to be encompassed. Thus, claims 33-38, 40, 42, 43, 46, 47, 51, 52, 58, 60, and 76 are not indefinite.

C. Third Rejection (Claim 76)

Claim 76 has been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite (Office Action, page 10). Applicants respectfully traverse this rejection.

The Examiner is of the opinion that:

> There are two grounds of rejection. Firstly, this is a compound claim, yet is dependant upon use claims 33, 42, 46, and 74. Secondly, do the substituted aryl and heteroaryl groups refer to the benzene and pyridine ring of Formula (III)? On the other hand, does this apply only to the aromatic rings of Groups R_{11}, R_{15}, and R_{16}?

Applicants respectfully disagree. Claim 76 as amended is a method claim dependent from claims 33, 42, and 46. The claim has also been amended to more clearly indicate that the optional substituents are on the R_{11}, R_{15}, and R_{16} groups.

Applicants respectfully submit that all of the stated grounds for the rejection of claims 33-43, 45-47, 51-58, 60, 71, and 74-77 under 35 U.S.C. § 112, second paragraph, have been traversed, accommodated or rendered moot. Therefore, Applicants respectfully submit that this rejection should be withdrawn.

Rejections Under 35 U.S.C. § 112, first paragraph

A. First Rejection (Claims 33-41 and 74)

Claims 33-41 and 74 have been rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not allegedly described in the specification in such a way as to enable one skilled in the art to use the invention. (Office Action, page 11).

Applicants respectfully traverse this rejection. The Examiner is of the opinion that "[t]he how to use portion of the statute means that Applicants must teach the skilled practitioner, in this case a physician, how to treat the claimed disease. The physician clearly must know what disease and what symptoms she is to treat." (Office Action page 11).

Applicants respectfully disagree. Claim 74 has been canceled. The claims as amended recite the specific disorders to be treated. It is well known to those of skill in the art what are the symptoms of these disorders and how the disorders may be treated as these disorders have been known and treated for many years by the skilled artisan. Although experimentation may be required to determine which of the compounds encompassed by the present invention are effective in treating each of the listed disorders, this experimentation is routine to the skilled artisan. The fact that the results of a clinical trail may possibly be inconclusive is not indicative of non-enablement in the absence of any evidence pointing to a reason why one of skill in the art would expect the results of trials of the claimed compounds to be inconclusive. Any inherent unpredictability in human disease treatment is insufficient to make a *prima facie* case for lack of enablement when one can routinely determine which treatments are effective or not effective. The discussion of Fas-ligand, psoralen, CD2 and Bcl-2 on pages 27-29 provides evidence that would be persuasive to one of skill in the art that apoptosis is involved in many disorders and that induction of apoptosis can lead to effective treatment of these disorders. Thus, a consideration of the *Forman* factors in light of the disclosures of the present specification does not lead one to a *prima facie* case of non-enablement. This conclusion is supported by the fact that the Examiner has not rejected any claims drawn to treatment of specific disorders (*i.e.*, claims 45, 54, 55, 57, 75). Thus, claims 33-41 are enabled.

B. Second Rejection (Claims 42, 43, 46, 47, 51, 52, 76, and 77)

Claims 42, 43, 46, 47, 51, 52, 76, and 77 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. (Office Action, page 12). Applicants respectfully traverse this rejection.

The Examiner is of the opinion that:

> Applicants are not enabled for "treating or preventing cancer" generally. There are two issues here. Firstly, [e]vidence involving a single compound and two types of cancer was not found sufficient to establish the enablement of claims directed to a method of treating seven types of cancer with members of a class of several compounds *In re Buting* 163 USPQ 689.

Applicants respectfully disagree. Claim 77 has been canceled. First, the claims do not encompass the prevention of cancer. This issue is therefore moot. Second, as discussed above, the claims as amended recite the specific cancers to be treated. One of skill in the art is very familiar with these cancers and their treatment. It would require no undue experimentation to determine which of the recited cancers can be treated by the compounds encompassed by the present invention. The Examiner, by not rejecting claim 45 for lack of enablement, has indicated that claims drawn to the treatment of specific cancers are enabled. Thus, claims 42, 43, 46, 47, 51, 52, and 76 are enabled.

C. Third Rejection (Claim 53)

Claim 53 has been rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one of skill in the art to make and/or use the invention. (Office Action, page 14). Applicants respectfully traverse this rejection.

Claim 53 has been canceled, thus rendering moot this basis for rejection.

D. Fourth Rejection (Claim 56)

Claim 56 was rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one of ordinary skill in the art to make and/or use the invention. (Office Action, page 17). Applicants respectfully traverse this rejection.

The Examiner is of the opinion that:

> The scope of "skin disease" cannot be deemed enabled. The term "skin disease" covers a broad array of different disorders that have different modes of action and different origins. The term would embrace such unrelated disorders as sun burn, acne, and melanoma. Under such circumstances, it is proper for the PTO to require evidence that such an unprecedented feat has actually been accomplished, *In re Ferens,* 163 USPQ 609.

Applicants respectfully disagree. Claim 56 has been canceled, thus rendering moot this basis for rejection.

E. Fifth Rejection (Claims 33-38, 40, 42, 43, 45-47, 51-58, 60, 71, and 75-77)

Claims 33-38, 40, 42, 43, 45-47, 51-58, 60, 71, and 75-77 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (Office Action, page 18). Applicants respectfully traverse this rejection.

The Examiner is of the opinion that:

> The provisos in the last ten lines of claims 33, 42, 46, the last three lines of claim 34, and the last two lines of claim 58 of claim 17 lack description. Nowhere in the specification is such a relationship linking the description among radicals R^1 through R^{11} described. Such a negative limitation requires description. In *Ex parte Grasselli, et al.* 231 USPQ 393, decided June 30, 1983, the U.S. Patent and Trademark Office, Board of Patent Appeals and Interferences said: "we agree with the examiner's position of record that the negative limitations recited in the present claims, which did not appear in the specification as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112." "It might be added that the express exclusion of certain elements implies the permissible inclusion of all other elements not so expressly excluded. This clearly illustrates that such negative limitations do, in fact, introduce new concepts."

Applicants respectfully disagree. Claims 45, 53-57, 75, and 77 have been canceled. *Ex parte Grasselli* is inapposite to the present issue as it does not relate to amendment of Markush groups. The controlling case law is *In re Johnson*, 194 U.S.P.Q. 187 (CCPA 1977), which indicates that deletion of individual members of Markush expression does not constitute new matter. The court said:

> the "written description" in the 1963 specification supported the claims in the absence of the limitation, and that

> specification, having described the whole, necessarily described the part remaining. The facts of the prosecution are properly presented and relied on, under these circumstances, to indicate that appellants are merely excising the invention of another, to which they are not entitled, and are not creating an "artificial subgenus" or claiming "new matter."

(*In re Johnson* at 196). Thus, there is adequate description of the claims in the specification.

F. Sixth Rejection (Claims 74, 76, and 77)

Claims 74, 76 and 77 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (Office Action, page 19). Applicants respectfully traverse this rejection.

Claims 74 and 77 have been canceled. Claim 76 as amended is not dependent from claim 74. Thus, the rejection has been rendered moot.

Applicants respectfully submit that the rejection of claims 33-43, 46, 47, 51-58, 60, 71, and 74-77 under 35 U.S.C. § 112, first paragraph have been traversed, accommodated or rendered moot. Therefore, Applicants respectfully submit that this rejection should be withdrawn.

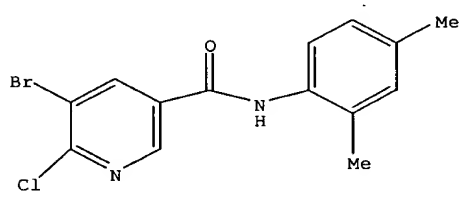
Rejections Under 35 U.S.C. § 102

The Examiner indicates that all of the anticipation rejections are maintained because the provisos inserted into the claims to exclude anticipatory compounds are new matter. Applicants respectfully disagree. As discussed above, *Ex parte Grasselli* is inapposite to the present issue as it does not relate to amendments to Markush groups. The controlling case law is *In re Johnson*, 194 U.S.P.Q. 187 (CCPA 1977), which indicates that deletion of individual members of Markush expression does not constitute new matter. Thus, there is adequate description of the claims in the specification.

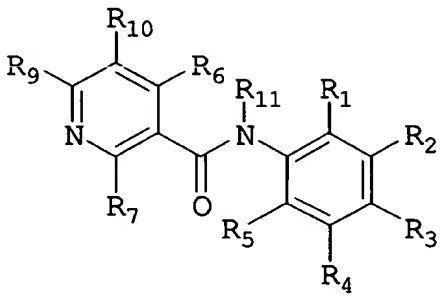
A. First Rejection (Claim 58)

Claim 58 has been rejected under 35 U.S.C. § 102(b) as being anticipated by Setliff (*Proc. Arkansas Acad. Sci.*) (Office Action, page 20). Applicants respectfully traverse this rejection. The Examiner is of the opinion that: "[t]he compound shown below fits Formula III with $R_1 = R_3 =$ methyl, $R_2 = R_4 = R_5 = R_6 = R_7 = R_{11} =$ hydrogen, $R_9 =$ chlorine, and $R_{10} =$ bromine." (Paper no. 4 at page 14, lines 2-3.) Applicants respectfully disagree.

Setliff discloses 5-bromo-6-chloro-N-(2,4-dimethylphenyl)-3-pyridinecarboxamide:



In contrast to the disclosure of Setliff, the compounds of the present invention are defined by the structure shown below.



(III)

The compound 5-bromo-6-chloro-N-(2,4-dimethylphenyl)-3-pyridinecarboxamide of Setliff has a methyl group in the position corresponding to R_1 and R_3 in the compounds of the present invention. In contrast to the compound disclosed in Setliff, both R_1 and R_3 cannot be alkyl in the compounds of the present invention. Therefore, Setliff does not anticipate claim 58. Applicants respectfully submit that the rejection has been overcome and should be withdrawn.

B. Second Rejection (Claim 58 and 71)

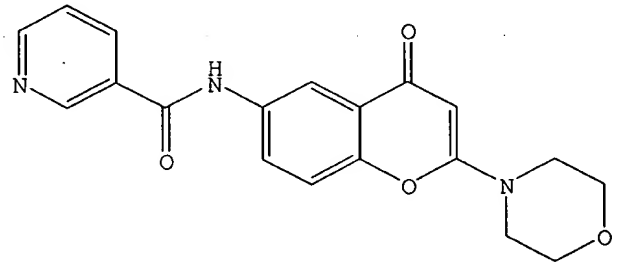
Claims 58 and 71 were rejected under 35 U.S.C. § 102(b) as being anticipated by Yagihara ('385 patent). (Office Action, page 20). Applicants respectfully traverse this rejection. The Examiner is of the opinion that: "[t]here are two compounds in this reference which anticipated Applicants compound and composition claims. The compound shown below fits Formula III with $R_1 = R_5$ = ethyl, R_3 = fluorine, $R_2 = R_4 = R_{11}$ = hydrogen, R_6 = chlorine, $R_7 = R_9$ = methyl, and R_{10} = isobutyl." (Paper no. 4 at page 14, lines 7-10.) Applicants respectfully disagree.

All compounds of Yagihara contain a halogen group in the position corresponding to R_6 in the present invention. In contrast, R_6 cannot be halogen in the compounds of the present invention. Therefore, Yagihara does not anticipate claims 58 and 71. Applicants respectfully submit that the rejection has been overcome and should be withdrawn.

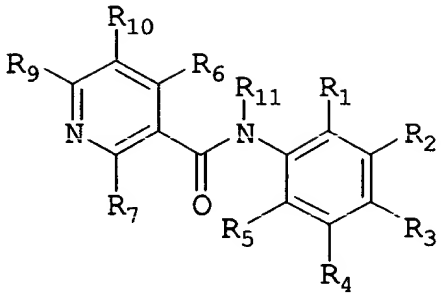
C. Third Rejection (Claim 33, 34, 36, 38, 42, 45, 46, 53, 54, 56, 57, 74, and 75)

Claim 33, 34, 36, 38, 42, 45, 53, 54, 56, 57, 74, and 75 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Gammill ('075 patent). (Office Action, page 20). Applicants respectfully traverse this rejection. The Examiner is of the opinion that: "[c]ompound 16 of the reference anticipated Applicant's use claims and fits formula (V) with Ar'=3-pyridyl and Ar = 2-(4-morpholinyl)-4H-benzopyran-4-on-6-yl. The compound is found in lines 54-55, column 20. Activity against cancer, arthritis, and psoriasis is disclosed in lines 11-24, column 16." (Paper no. 4 at page 15, lines 2-6.) Applicants respectfully disagree.

Gammill discloses, 6-(3-pyridinecarboxamide)-2-(4-morpholinyl)-4H-1-benzopyran-4-one:



In contrast to the disclosure of Gammill, the compounds of the invention are defined by the structure shown below.



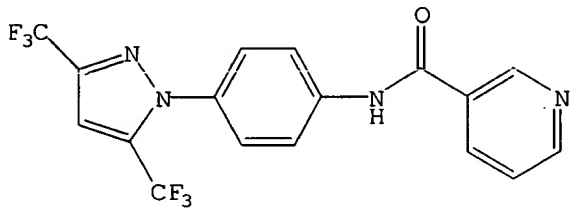
(III)

Claims 53, 54, 56, 57, 74, and 75 have been canceled. According to Gammill, the portion of the molecule corresponding to R_2 taken together with R_3 is 2-morpholine-pyran-4-one. In contrast, the compounds of the invention can have R_2 and R_3 taken together to form a heterocycle, but not optionally substituted pyran-4-one (*see, e.g.*, claims 33, 42 and 46). Therefore, Gammill does not anticipate claims 33, 34, 36, 38, 42, and 46. Applicants respectfully submit that the rejection has been overcome and should be withdrawn.

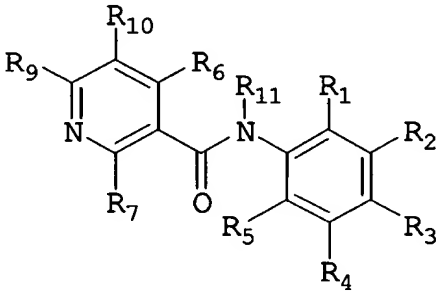
D. Fourth Rejection (Claims 33, 36, 38, 53, 54, 74 and 75)

Claims 33, 36, 38, 53, 54, 74 and 75 have been rejected 35 U.S.C. § 102(a) as being anticipated by Kubotab [sic, Kubota] (WO 99/19303 A1). (Office Action, page 20). Applicants respectfully traverse this rejection. The Examiner is of the opinion that "[t]here is one compound in this reference, which anticipates Applicants' use claims. There is one compound in this reference, which anticipates Applicants' use claims. It is entry 36 on page 36. It and [sic] fits formula (III) with $R_6 = R_7 = R_9 = R_{10}$ = hydrogen, $R_1 = R_2 = R_4 = R_5$ = hydrogen, and R_3 = 3,5-bis(trifluoromethyl)-1H-pyrazol-l-yl. Activity against autoimmune diseases and rheumatoid arthritis is taught in the abstract." Applicants respectfully disagree.

Kubota discloses 4-[3,5-(bistrifluoromethyl)-1H-pyrazol-1-yl]-phenyl-3-pyridinecarboxamide:



In contrast to Kubota, the compounds disclosed in the present invention are defined by the structure shown below.



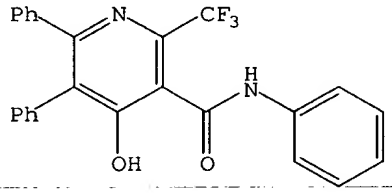
(III)

Claims 53, 54, 74, and 75 have been canceled. The compounds of Kubota have a 1H-pyrazolyl group corresponding to the group R_3 in the present invention. In contrast to the disclosure of Kubota, compounds of the present invention cannot have optionally substituted pyrazolyl as R_3 when R_{1-2} and R_{4-11} are hydrogen. Kubota, therefore, does not anticipate claims 33, 36, and 38. Applicants respectfully submit that the rejection has been overcome and should be withdrawn.

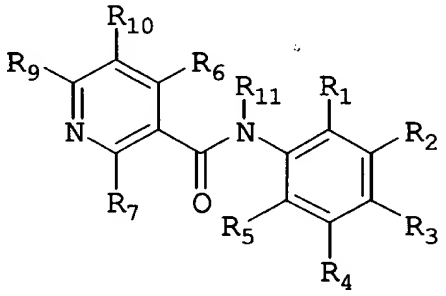
E. Fifth rejection (Claims 33, 38, 53, 54, 74, and 75)

Claims 33, 38, 53, 54, 74, and 75 were rejected under 35 U.S.C. § 102(b) as being anticipated by Clémence ('140 patent). (Office Action, page 21). Applicants respectfully traverse this rejection. The Examiner is of the opinion that "[t]here is one compound in this reference, which anticipates Applicant's use claims. The compound was cited previously and fits formula (III) with R_6 = hydroxy, R_7 = trifluoromethyl, R_9 = R_{10} = phenyl and R_1 = R_2 = R_3 = R_4 = R_5 = hydrogen. It is Example 4, lines 13, column 10 to line 43, column 11. Activity against rheumatoid arthritis is taught in the claim 15 of the reference." Applicants respectfully disagree.

Clémence discloses the compound 4-hydroxy-5,6-diphenyl-2-trifluoromethyl-N-phenyl-3-pyridinecarboximide:



In contrast to Clémence, compounds of the present invention are represented by Formula III:



(III)

Claims 53, 54, 74, and 75 have been canceled. The compounds of the invention, as defined by Formula (III), do not include compounds wherein both R_9 and R_{10} are phenyl and R_{1-5} are hydrogen. Therefore, Clémence does not anticipate claims 33 and 38. Applicants respectfully submit the rejection has been overcome and should be withdrawn.

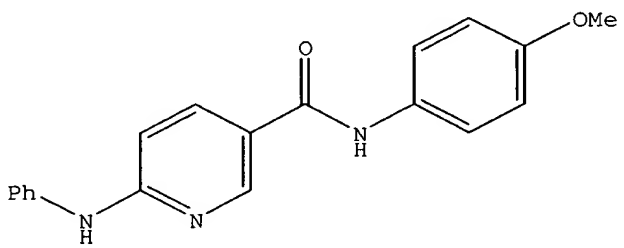
F. Sixth rejection (Claims 33, 36, 38, 42, 45, 46, 53-57, 74 and 75)

Claims 33, 36, 38, 42, 45, 46, 53-57, 74 and 75 were rejected under 35 U.S.C. § 102(e) as being anticipated by Mantlo ('884 patent). (Office Action, page 21). Applicants respectfully traverse this rejection. Specifically, the Examiner is of the opinion that:

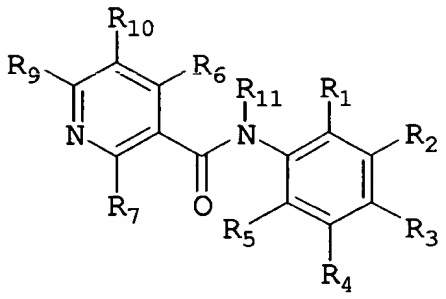
> There are over one hundred compounds disclosed in this reference, which anticipate Applicant's use claims. One compound was previously cited and fits formula (III) with R6 = R7 = R10 = hydrogen, R9 = phenylamino, R1 = R2 = R4 = R5 = hydrogen, and R3 = methoxy. The compounds are found in Tables 8-13, spanning columns 84-91. See also compound claims 1-15 in this reference. Activity against rheumatoid arthritis is taught in line 36, column 96 of the reference. Activity against inflammatory bowel disease and psoriasis is taught in line 40-41, column 96. Activity against cancer is taught in line 57, column 96.

Applicants respectfully disagree.

Mantlo discloses, for example, 6-(phenylamino)-N-(4-methoxyphenyl)-3-pyridinecarboxamide:



In contrast to Mantlo, compounds of the present invention are represented by Formula III:



(III)

Claims 45, 53-57, 74, and 75 have been canceled. All the relevant compounds disclosed in Mantlo have an N-substituted amino group corresponding to the group R_9 in the present invention. The relevant compounds in Mantlo are N-substituted by aryl or cycloalkyl groups. In contrast to the disclosure of Mantlo, the compounds of the present invention cannot have R_9 be amino substituted by aryl or cycloalkyl groups. Mantlo, therefore, does not anticipate claims 33, 36, 38, 42, and 46. Applicants respectfully submit that the rejection has been overcome and should be withdrawn.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite

prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Robert A. Schwartzman
Agent for Applicants
Registration No. 50,211

Date: 1/7/03

1100 New York Avenue, N.W.
Suite 600
Washington, D.C. 20005-3934
(202) 371-2600

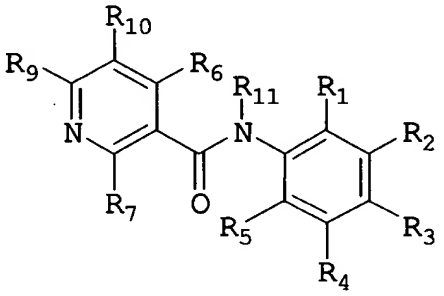
Version with markings to show changes made

In the Claims:

Claims 45, 49, 50, 53-57, 72-75, and 77 were canceled without prejudice or disclaimer to the subject matter thereof.

Claims 33, 42, 43, 46, 47, 58, and 76 were amended as follows:

33. (Twice Amended) A method of treating a disorder responsive to the induction of apoptosis in an animal suffering therefrom, comprising administering to a mammal in need of such treatment an effective amount of a compound of Formula III:



(III)

or a pharmaceutically acceptable salt or prodrug thereof, wherein

R_1-R_7 and R_9-R_{10} are independently hydrogen, halo, haloalkyl, haloalkoxy, aryl, fused aryl, carbocyclic, fused carbocyclic, a heterocyclic group, fused heterocyclic, a heteroaryl group, alkyl, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl, nitro, aminoalkyl, cyano, cyanoalkyl, acyl, acylamido, hydroxy, thiol, acyloxy, azido, alkoxy, alkoxycarbonyl, aryloxy, arylalkoxy, carboxy, carbonylamido or alkylthiol, $-NH_2$, $-NHR_{15}$ or $-NR_{15}R_{16}$, wherein

R_{15} and R_{16} are independently optionally substituted $C_{1\text{-}10}$ alkyl, heterocyclic or heteroaryl groups; and

R_{11} is hydrogen; or alkyl, cycloalkyl, aryl or heteroaryl, each of which is optionally substituted;

wherein said disorder responsive to the induction of apoptosis is inflammatory bowel disease, psoriasis, an autoimmune disease selected from the group consisting of rheumatoid arthritis, multiple sclerosis, diabetes mellitus, Hashimoto's thyroiditis, and autoimmune lymphoproliferative syndrome, or a cancer selected from the group consisting of Hodgkin's disease, non-Hodgkin's lymphoma, acute lymphocytic leukemia, chronic lymphocytic leukemia, multiple myeloma, neuroblastoma, breast carcinoma, ovarian carcinoma, lung carcinoma, Wilms' tumor, cervical carcinoma, testicular carcinoma, soft-tissue sarcoma, primary macroglobulinemia, bladder carcinoma, chronic granulocytic leukemia, primary brain carcinoma, malignant melanoma, small-cell lung carcinoma, stomach carcinoma, colon carcinoma, malignant pancreatic insulinoma, malignant carcinoid carcinoma, choriocarcinoma, mycosis fungoides, head or neck carcinoma, oesteogenic sarcoma, pancreatic carcinoma, acute granulocytic leukemia, hairy cell leukemia, rhabdomyosarcoma, Kaposi's sarcoma, genitourinary carcinoma, thyroid carcinoma, esophageal carcinoma, malignant hypercalcemia, cervical hyperplasia, renal cell carcinoma, endometrial carcinoma, polycythemia vera, essential thrombocytosis, adrenal cortex carcinoma, skin cancer and prostatic carcinoma; and

wherein said prodrug is:

a) an ester of a carboxylic acid containing compound of Formula III obtained by condensation with a C_{1-4} alcohol;

b) an ester of a hydroxyl group containing compound of Formula III obtained by condensation with a C_{1-4} carboxylic acid, C_{3-6} dioic acid or anhydride thereof;

c) an imine of an amine group containing compound of Formula III obtained by condensation with a C_{1-4} aldehyde or ketone; or

d) an acetal or ketal of at least one of the R_{1-10} hydroxy containing groups obtained by condensation with chloromethyl methyl ether or chloromethyl ethyl ether;

provided that:

when R_{1-2} and R_{4-11} are hydrogen, R_3 is not optionally substituted pyrazolyl;

when R_{1-5} are hydrogen, each of R_9 and R_{10} are not phenyl;

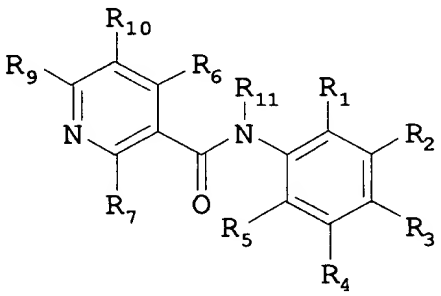
when R_3 is methoxy and R_{5-11} are hydrogen, each of R_2 and R_4 are not cyclopentyloxy;

when R_{1-3} and R_{5-11} are hydrogen, R_4 is not optionally substituted alkyl;

when R_{3-11} are hydrogen, R_1 and R_2 are not taken together to form optionally substituted thienyl-1,1-dioxide or partially saturated thienyl-1,1-dioxide; and

when R_1 and R_{4-11} are hydrogen, R_2 and R_3 are not taken together to form substituted pyranyl.

42. (Twice Amended) A method for treating cancer, comprising administering to an animal in need of such treatment an effective amount of a compound of Formula III:



(III)

or a pharmaceutically acceptable salt or prodrug thereof, wherein:

R_1-R_7 and R_9-R_{10} are independently hydrogen, halo, haloalkyl, haloalkoxy, aryl, fused aryl, carbocyclic, fused carbocyclic, a heterocyclic group, fused heterocyclic, a heteroaryl group, alkyl, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl, nitro, aminoalkyl, cyano, cyanoalkyl, acyl, acylamido, hydroxy, thiol, acyloxy, azido, alkoxy, alkoxycarbonyl, aryloxy, arylalkoxy, carboxy, carbonylamido or alkylthiol, $-NH_2$, $-NHR_{15}$ or $-NR_{15}R_{16}$, wherein

R_{15} and R_{16} are independently optionally substituted C_{1-10} alkyl, heterocyclic or heteroaryl groups; and

R_{11} is hydrogen; or alkyl, cycloalkyl, aryl or heteroaryl, each of which is optionally substituted;

wherein said cancer is selected from the group consisting of Hodgkin's disease, non-Hodgkin's lymphoma, acute lymphocytic leukemia, chronic lymphocytic leukemia, multiple myeloma, neuroblastoma, breast carcinoma, ovarian carcinoma, lung carcinoma, Wilms' tumor, cervical carcinoma, testicular carcinoma, soft-tissue sarcoma, primary macroglobulinemia, bladder carcinoma, chronic granulocytic leukemia, primary brain carcinoma, malignant melanoma, small-cell lung carcinoma, stomach carcinoma, colon carcinoma, malignant pancreatic insulinoma, malignant carcinoid carcinoma, choriocarcinoma, mycosis fungoides, head or neck carcinoma, oesteogenic sarcoma, pancreatic carcinoma, acute granulocytic leukemia, hairy cell leukemia, rhabdomyosarcoma, Kaposi's sarcoma, genitourinary carcinoma, thyroid carcinoma, esophageal carcinoma, malignant hypercalcemia, cervical hyperplasia, renal cell carcinoma, endometrial carcinoma, polycythemia vera, essential thrombocytosis, adrenal cortex carcinoma, skin cancer and prostatic carcinoma; and

wherein said prodrug is:

a) an ester of a carboxylic acid containing compound of Formula III obtained by condensation with a C_{1-4} alcohol;

b) an ester of a hydroxyl group containing compound of Formula III obtained by condensation with a C_{1-4} carboxylic acid, C_{3-6} dioic acid or anhydride thereof;

c) an imine of an amine group containing compound of Formula III obtained by condensation with a C_{1-4} aldehyde or ketone; or

d) an acetal or ketal of at least one of the R_{1-10} hydroxy containing groups obtained by condensation with chloromethyl methyl ether or chloromethyl ethyl ether;

provided that:

when R_{1-2} and R_{4-11} are hydrogen, R_3 is not optionally substituted pyrazolyl;

when R_{1-5} are hydrogen, each of R_9 and R_{10} are not phenyl;

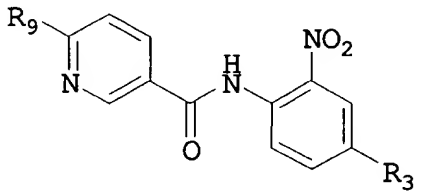
when R_3 is methoxy and R_{5-11} are hydrogen, each of R_2 and R_4 are not cyclopentyloxy;

when R_{1-3} and R_{5-11} are hydrogen, R_4 is not alkyl;

when R_{3-11} are hydrogen, R_1 and R_2 are not taken together to form optionally substituted thienyl-1,1-dioxide or partially saturated thienyl-1,1-dioxide; and

when R_1 and R_{4-11} are hydrogen, R_2 and R_3 are not taken together to form substituted pyranyl.

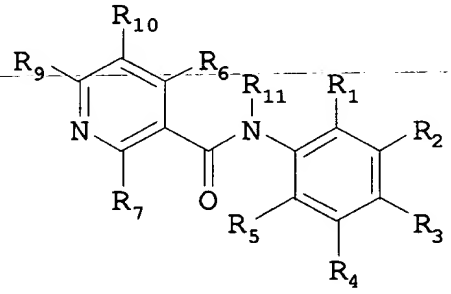
43. (Twice Amended) The method of claim 42, wherein said compound is of Formula IV:



(IV)

or a pharmaceutically acceptable salt [salts] or prodrug [prodrugs] thereof.

46. (Twice Amended) A method for the treatment of drug resistant cancer, comprising administering to an animal in need of such treatment an effective amount of a compound of the Formula III:



(III)

or a pharmaceutically acceptable salt or prodrug thereof, wherein:

R_1-R_7 and R_9-R_{10} are independently hydrogen, halo, haloalkyl, haloalkoxy, aryl, fused aryl, carbocyclic, fused carbocyclic, a heterocyclic group, fused heterocyclic, a heteroaryl group, alkyl, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl, nitro, aminoalkyl, cyano, cyanoalkyl, acyl, acylamido, hydroxy, thiol,

acyloxy, azido, alkoxy, alkoxycarbonyl, aryloxy, arylalkoxy, carboxy, carbonylamido or alkylthiol, $-NH_2$, $-NHR_{15}$ or $-NR_{15}R_{16}$, wherein

R_{15} and R_{16} are independently optionally substituted C_{1-10} alkyl, heterocyclic or heteroaryl groups; and

R_{11} is hydrogen; or alkyl, cycloalkyl, aryl or heteroaryl, each of which is optionally substituted;

wherein said drug resistant cancer is selected from the group consisting of Hodgkin's disease, non-Hodgkin's lymphoma, acute lymphocytic leukemia, chronic lymphocytic leukemia, multiple myeloma, neuroblastoma, breast carcinoma, ovarian carcinoma, lung carcinoma, Wilms' tumor, cervical carcinoma, testicular carcinoma, soft-tissue sarcoma, primary macroglobulinemia, bladder carcinoma, chronic granulocytic leukemia, primary brain carcinoma, malignant melanoma, small-cell lung carcinoma, stomach carcinoma, colon carcinoma, malignant pancreatic insulinoma, malignant carcinoid carcinoma, choriocarcinoma, mycosis fungoides, head or neck carcinoma, oesteogenic sarcoma, pancreatic carcinoma, acute granulocytic leukemia, hairy cell leukemia, rhabdomyosarcoma, Kaposi's sarcoma, genitourinary carcinoma, thyroid carcinoma, esophageal carcinoma, malignant hypercalcemia, cervical hyperplasia, renal cell carcinoma, endometrial carcinoma, polycythemia vera, essential thrombocytosis, adrenal cortex carcinoma, skin cancer and prostatic carcinoma; and

wherein said prodrug is:

a) an ester of a carboxylic acid containing compound of Formula III obtained by condensation with a C_{1-4} alcohol;

b) an ester of a hydroxyl group containing compound of Formula III obtained by condensation with a C_{1-4} carboxylic acid, C_{3-6} dioic acid or anhydride thereof;

c) an imine of an amine group containing compound of Formula III obtained by condensation with a C_{1-4} aldehyde or ketone; or

d) an acetal or ketal of at least one of the R_{1-10} hydroxy containing groups obtained by condensation with chloromethyl methyl ether or chloromethyl ethyl ether;

provided that:

when R_{1-2} and R_{4-11} are hydrogen, R_3 is not optionally substituted pyrazolyl;

when R_{1-5} are hydrogen, each of R_9 and R_{10} are not phenyl;

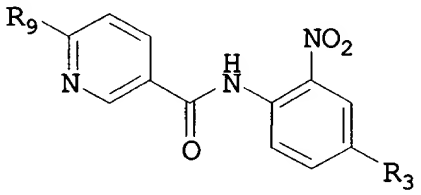
when R_3 is methoxy and R_{5-11} are hydrogen, each of R_2 and R_4 are not cyclopentyloxy;

when R_{1-3} and R_{5-11} are hydrogen, R_4 is not alkyl;

when R_{3-11} are hydrogen, R_1 and R_2 are not taken together to form optionally substituted thienyl-1,1-dioxide or partially saturated thienyl-1,1-dioxide; and

when R_1 and R_{4-11} are hydrogen, R_2 and R_3 are not taken together to form substituted pyranyl.

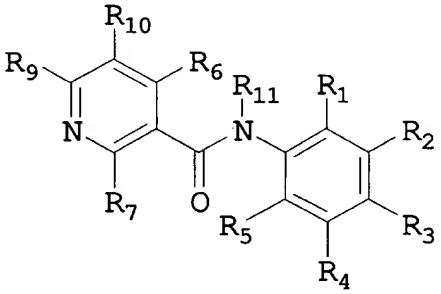
47. (Twice Amended) The method of claim 46, wherein said compound is of Formula IV:



(IV)

or a pharmaceutically acceptable salt [salts] or prodrug [prodrugs] thereof.

58. (Twice Amended) A compound of Formula III:



(III)

or a pharmaceutically acceptable salt or prodrug thereof, wherein:

R_1 and R_5 are independently selected from the group consisting of hydrogen, hydroxy, alkyl, alkoxy, halogen, NO_2, cyano, haloalkyl, haloalkoxy, amino and

aminoalkyl, provided that at least one of R_1 and R_5 is selected from the group consisting of NO_2, cyano, alkyl and haloalkyl;

R_2 and R_4 are independently selected from the group consisting of hydrogen, hydroxy, halogen, cyano, haloalkyl, haloalkoxy, amino and aminoalkyl;

R_3 is alkyl, Cl, F, haloalkyl, alkoxy, arylalkoxy, cyano, haloalkyloxy, amino or aminoalkyl;

R_6 is hydrogen, hydroxy, alkyl, NO_2, cyano, haloalkyl, haloalkyloxy, amino or aminoalkyl;

R_7 is hydrogen, hydroxy, alkyl, NO_2, cyano, haloalkyl, haloalkyloxy, amino or aminoalkyl;

R_9 is hydroxy, alkyl, halogen, NO_2, haloalkyl, alkoxy, cyano, haloalkyloxy, amino or aminoalkyl;

R_{10} is hydrogen, hydroxy, alkyl, Cl, F, NO_2, cyano, haloalkyl, haloalkyloxy, amino or aminoalkyl; and

R_{11} is hydrogen, alkyl or haloalkyl;

wherein said prodrug is:

a) an ester of a carboxylic acid containing compound of Formula III obtained by condensation with a C_{1-4} alcohol;

b) an ester of a hydroxyl group containing compound of Formula III obtained by condensation with a C_{1-4} carboxylic acid, C_{3-6} dioic acid or anhydride thereof;

c) an imine of an amine group containing compound of Formula III obtained by condensation with a C_{1-4} aldehyde or ketone; or

d) an acetal or ketal of at least one of the R_{1-10} hydroxy containing groups obtained by condensation with chloromethyl methyl ether or chloromethyl ethyl ether;

provided that when R_2 and R_4 are hydrogen and R_{9-10} are halo, R_1 or R_5 and R_3 are not both alkyl.

76. (Once Amended) The method [compound] of any one of claims 33, 42, and 46 [,58 and 72] wherein optional substituents on the alkyl or heteroaryl group of R_{15}

and R_{16} or the alkyl, aryl, or heteroaryl group of R_{11} [aryl, aralkyl and heteroaryl groups] include one or more halo, C_1-C_6 haloalkyl, C_6-C_{10} aryl, C_4-C_7 cycloalkyl, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_6-C_{10} aryl(C_1-C_6)alkyl, C_6-C_{10} aryl(C_2-C_6)alkenyl, C_6-C_{10} aryl(C_2-C_6)alkynyl, C_1-C_6 hydroxyalkyl, nitro, amino, ureido, cyano, C_1-C_6 acylamino, hydroxy, thiol, C_1-C_6 acyloxy, azido, C_1-C_6 alkoxy or carboxy.